

WHAT IS CLAIMED IS:

1. A purified polypeptide, comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:6; where amino acid residue 73, as represented by Xaa, is Ile or Thr;

(b) a contiguous fragment of SEQ ID NO:6, which fragment induces interferon- γ production in immunocompetent human cells; and

(c) a variant of (a) or (b) differing therefrom by replacement of one amino acid residue, which variant induces interferon- γ production in immunocompetent human cells.

2. The purified polypeptide of claim 1, which has a molecular weight of about $18,500 \pm 3,000$ daltons on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and an isoelectric point of about 4.9 ± 1.0 on chromatofocusing.

3. The purified polypeptide of claim 1, which comprises the amino acid sequence of SEQ ID NO:6, where Xaa at residue 73 is isoleucine or threonine.

4. The purified polypeptide of claim 1, which comprises the amino acid sequence of a contiguous fragment of SEQ ID NO:6, where amino acid residue 73, as represented by Xaa, is Ile or Thr, which fragment induces interferon- γ production in immunocompetent human cells.

5. The purified polypeptide of claim 1, which comprises a variant of (a) or (b) differing therefrom by

replacement of one amino acid residue, which variant induces interferon- γ production in immunocompetent cells.

6. A pharmaceutical composition, comprising the polypeptide of claim 1 as an active ingredient and a pharmaceutically-acceptable carrier.

7. The pharmaceutical composition of claim 6, further comprising interleukin 2.

8. The pharmaceutical composition of claim 6, further comprising interleukin 12.

9. The pharmaceutical composition of claim 6, further comprising interleukin 3.

10. A method for treating atopic diseases, tumors, viral diseases, bacterial diseases, or immunopathies, comprising administering to a patient in need thereof an effective amount of the polypeptide of claim 1.

11. A method for treating malignant lymphoma, comprising:

contacting mononuclear cells isolated from peripheral blood of a patient with malignant lymphoma with a combination of the polypeptide of claim 1 and interleukin 2;

culturing the mononuclear cells,

collecting LAK cells; and

introducing the collected LAK cells into the patient to exhibit cytotoxicity on malignant lymphoma cells.

12. A method for treating tumors, comprising:

contacting lymphocytes obtained from tumor tissues of a patient with a combination of the polypeptide of claim 1 and interleukin 2;

culturing the lymphocytes;

collecting cytotoxic T cells; and

introducing the collected cytotoxic T cells into the patient to exhibit cytotoxicity on tumor cells.

13. A method for treating leukopenia or thrombocytopenia, comprising administering the polypeptide of claim 1 and interleukin 3 to a subject in need thereof.

14. A method for enhancing the cytotoxicity of NK cells, comprising contacting NK cells with the polypeptide of claim 1 to enhance the cytotoxicity of NK cells.

15. The method of claim 14, wherein said NK cells are also contacted with interleukin 2.

16. A method for inducing the formation of LAK cells, comprising contacting LAK cell-containing lymphocytes with the polypeptide of claim 1 to induce the formation of LAK cells.

17. The method of claim 16, wherein said lymphocytes are also contacted with interleukin 2.

18. A pharmaceutical composition, comprising:
an interferon- γ inducing polypeptide which is a polypeptide of SEQ ID NO:6 obtainable from humans, where amino acid residue 73 of SEQ ID NO:6, as represented by Xaa, is Ile or Thr, or a fragment thereof, or a homologous polypeptide thereof, wherein the fragment has substantially the same interferon- γ

inducing activity as the polypeptide of SEQ ID NO:6, and the polypeptide of SEQ ID NO:6 and the homologous polypeptide thereof has the following physicochemical properties:

- Sub. 32*
- (1) an amino acid sequence selected from the group consisting of SEQ ID NO:6, where amino acid residue 73, as represented by Xaa, is Ile or Thr, and a homologous sequence thereof where at least one amino acid residue in SEQ ID NO:6 is replaced with a different amino acid, or at least one amino acid residue is added to or deleted from the N-terminus and/or the C-terminus of SEQ ID NO:6, wherein said homologous polypeptide has substantially the same physicochemical properties and biological activity as the polypeptide of SEQ ID NO:6,
 - (2) molecular weight
18,500 \pm 3,000 daltons on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE);
 - (3) isoelectric point (pI)
4.9 \pm 1.0 on chromatofocusing;
 - (4) biological activity
inducing interferon- γ production by human immunocompetent cells; and
 - (5) acute toxicity
having an LD₅₀ of at least about one mg/kg when tested in mice;

a biologically active compound; and
a pharmaceutically acceptable carrier, adjuvant,
excipient, diluent, and/or stabilizer.

Sub. B2
19. The pharmaceutical composition of claim 18,
wherein said interferon- γ inducing polypeptide is the polypeptide
of SEQ ID NO:6, where residue 73, as represented by Xaa, is Ile
or Thr, or a biologically active fragment thereof.

20. The pharmaceutical composition of claim 18,
wherein said interferon- γ inducing polypeptide is said homologous
polypeptide.

21. The pharmaceutical composition of claim 18,
wherein said biologically active compound is selected from the
group consisting of interferon- α , interferon- β , interleukin 2,
interleukin 3, interleukin 12, TNF- α , TNF- β , carboquone,
cyclophosphamide, aclarubicin, thiotepa, busulfan, ancitabine,
cytarabine, 5-fluorouracil, 5-fluoro-1-(tetrahydro-2-furyl)
uracil, methotrexate, actinomycin D, chromomycin A3,
daunorubicin, doxorubicin, bleomycin, mitomycin C, vincristine,
vinblastine, L-asparaginase, radio gold colloidal, Krestin®,
picibanil, lentinan, Maruyama vaccine, and mixtures thereof.

22. The pharmaceutical composition of claim 21,
wherein said biologically active compound is interferon- α .

23. The pharmaceutical composition of claim 21,
wherein said biologically active compound is interferon- β .

24. The pharmaceutical composition of claim 21,
wherein said biologically active compound is interleukin 2.

25. The pharmaceutical composition of claim 21, wherein said biologically active compound is interleukin 3.

26. The pharmaceutical composition of claim 21, wherein said biologically active compound is interleukin 12.

27. The pharmaceutical composition of claim 21, wherein said biologically active compound is TNF- α .

28. The pharmaceutical composition of claim 21, wherein said biologically active compound is TNF- β .

29. The pharmaceutical composition of claim 21, wherein said biologically active compound is carboquone.

30. The pharmaceutical composition of claim 21, wherein said biologically active compound is cyclophosphamide.

31. The pharmaceutical composition of claim 21, wherein said biologically active compound is aclarubicin.

32. The pharmaceutical composition of claim 21, wherein said biologically active compound is thiotepa.

33. The pharmaceutical composition of claim 21, wherein said biologically active compound is busulfan.

34. The pharmaceutical composition of claim 21, wherein said biologically active compound is ancitabine.

35. The pharmaceutical composition of claim 21, wherein said biologically active compound is cytarabine.

36. The pharmaceutical composition of claim 21, wherein said biologically active compound is 5-fluorouracil.

37. The pharmaceutical composition of claim 21, wherein said biologically active compound is 5-fluoro-1-(tetrahydro-2-furyl) uracil.

38. The pharmaceutical composition of claim 21, wherein said biologically active compound is methotrexate.

39. The pharmaceutical composition of claim 21, wherein said biologically active compound is actinomycin D.

40. The pharmaceutical composition of claim 21, wherein said biologically active compound is chromomycin A3.

41. The pharmaceutical composition of claim 21, wherein said biologically active compound is daunorubicin.

42. The pharmaceutical composition of claim 21, wherein said biologically active compound is doxorubicin.

43. The pharmaceutical composition of claim 21, wherein said biologically active compound is bleomycin.

44. The pharmaceutical composition of claim 21, wherein said biologically active compound is mitomycin C.

45. The pharmaceutical composition of claim 21, wherein said biologically active compound is vincristine.

46. The pharmaceutical composition of claim 21, wherein said biologically active compound is vinblastine.

47. The pharmaceutical composition of claim 21, wherein said biologically active compound is L-asparaginase.

48. The pharmaceutical composition of claim 21, wherein said biologically active compound is radio gold colloidal.

49. The pharmaceutical composition of claim 21, wherein said biologically active compound is Krestin®.

50. The pharmaceutical composition of claim 21, wherein said biologically active compound is picibanil.

51. The pharmaceutical composition of claim 21, wherein said biologically active compound is lentinan.

52. The pharmaceutical composition of claim 21, wherein said biologically active compound is Maruyama vaccine.

53. A pharmaceutical composition for inducing human interferon- γ , enhancing cytotoxicity of human killer cells and/or inducing formation of human killer cells, comprising a pharmaceutically acceptable carrier, and as an effective ingredient, 0.000001 w/w % to 100 w/w % on a dry solid basis of a polypeptide of SEQ ID NO:6 obtainable from humans, where amino acid residue 73 of SEQ ID NO:6, as represented by Xaa, is Ile or Thr, or a homologous polypeptide thereof, wherein the polypeptide and the homologous polypeptide thereof has the following physicochemical properties:

- (a) an amino acid sequence selected from the group consisting of SEQ ID NO:6, where amino acid residue 73, as represented by Xaa, is Ile or Thr, and a homologous sequence thereof where at least one amino acid residue in SEQ ID NO:6 is replaced with a different amino acid, or at least one amino acid residue is added to or deleted from the N-terminus and/or the C-terminus of SEQ ID NO:6, wherein said

homologous polypeptide has substantially the same physicochemical properties and biological activity as the polypeptide of SEQ ID NO:6;

(b) Molecular weight

18,500 \pm 3,000 daltons on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(c) Isoelectric point (pI)

4.9 \pm 1.0 on chromatofocusing;

(d) Biological activity.

54. The pharmaceutical composition of claim 53, further comprising a stabilizer selected from the group consisting of serum albumin, gelatin, maltose, and trehalose.

55. The pharmaceutical composition of claim 53, wherein the killer cells are selected from the group consisting of natural killer cells, lymphokine-activating killer cells, and cytotoxic T-cells.

56. The pharmaceutical composition of claim 53, wherein said effective ingredient is the homologous polypeptide.

57. The pharmaceutical composition of claim 56, further comprising at least one member selected from the group consisting of interleukin 2 and concanavalin A.

58. The pharmaceutical composition of claim 53, wherein said effective ingredient is the polypeptide of SEQ ID NO:6, where amino acid residue 73, as represented by Xaa, is Ile or Thr.

59. The pharmaceutical composition of claim 58, further comprising at least one member selected from the group consisting

of stabilizer, adjuvants, excipients, diluents, and biologically-active substances.

60. The pharmaceutical composition of claim 59, wherein said biologically-active substance is at least one member selected from the group consisting of interleukins, interferons, tumor necrosis factors, and antitumor agents.

61. The pharmaceutical composition of claim 59, wherein said stabilizer is at least one member selected from the group consisting of serum albumin, gelatin, maltose, and trehalose.

62. A method for treating viral diseases, bacterial diseases, immune diseases, cancer, and atopic disorders, comprising administering to a patient in need thereof an effective amount of an interferon- γ inducing polypeptide which is a polypeptide of SEQ ID NO:6 obtainable from humans, where amino acid residue 73 of SEQ ID NO:6, as represented by Xaa, is Ile or Thr, or a fragment thereof, or a homologous polypeptide thereof, wherein the fragment has substantially the same interferon- γ inducing activity as the polypeptide of SEQ ID NO:6, and the polypeptide of SEQ ID NO:6 and the homologous polypeptide thereof has the following physicochemical properties:

- (a) an amino acid sequence selected from the group consisting of SEQ ID NO:6, where amino acid residue 73, as represented by Xaa, is Ile or Thr, and a homologous sequence thereof where at least one amino acid residue in SEQ ID NO:6 is replaced with a different amino acid, or at least one amino acid

residue is added to or deleted from the N-terminus and/or the C-terminus of SEQ ID NO:6, wherein said homologous polypeptide has substantially the same physicochemical properties and biological activity as the polypeptide of SEQ ID NO:6,

(b) molecular weight

18,500 \pm 3,000 daltons on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(c) isoelectric point (pI)

4.9 \pm 1.0 on chromatofocusing;

(d) biological activity

inducing IFN- γ production by human immunocompetent cells; and

(e) acute toxicity

having an LD₅₀ of at least about one mg/kg when tested in mice.

63. The method of claim 62, wherein the patient in need thereof is suffering from a viral disease.

64. The method of claim 63, wherein the viral disease is selected from the group consisting of hepatitis, herpes syndrome, condyloma, and AIDS.

65. The method of claim 62, wherein the patient in need thereof is suffering from a bacterial disease.

66. The method of claim 65, wherein the bacterial disease is selected from the group consisting of candidiasis and malaria.

67. The method of claim 62, wherein the patient in need thereof is suffering from an immune disease.

68. The method of claim 67, wherein the immune disease is selected from the group consisting of allergy and rheumatism.

69. The method of claim 62, wherein the patient in need thereof is suffering from cancer.

70. The method of claim 69, wherein the cancer is selected from the group consisting of renal cancer, mycosis fungoides, chronic granulomatous disease, adult T cell leukemia, chronic myelogenous leukemia, and malignant leukemia.

71. The method of claim 69, wherein the cancer is leukemia or myeloma and further comprises administering an effective amount of interleukin 3.

72. The method of claim 62, further comprising administering an effective amount of a biologically active compound selected from the group consisting of interferon- α , interferon- β , interleukin 2, interleukin 3, interleukin 12, TNF- α , TNF- β , carboquone, cyclophosphamide, aclarubicin, thiotepa, busulfan, ancitabine, cytarabine, 5-fluorouracil, 5-fluoro-1-(tetrahydro-2-furyl) uracil, methotrexate, actinomycin D, chromomycin A3, daunorubicin, doxorubicin, bleomycin, mitomycin C, vincristine, vinblastine, L-asparaginase, radio gold colloidal, Krestin®, picibanil, lentinan, and Maruyama vaccine, and mixtures thereof.

73. The method of claim 72, wherein the biologically active compound is interleukin 12.

74. The method of claim 73, wherein the patient in need thereof is suffering from an atopic disorder.

75. The method of claim 74, wherein the atopic disorder is selected from the group consisting of allergic asthma, atopic bronchial asthma, hay fever, allergic rhinitis, atopic dermatitis, vascular edema, and atopic disorders of the digestive system.

76. The method of claim 72, wherein the biologically active compound is interleukin 2.

77. A method for treating leukopenia or thrombopenia, comprising administering to a patient in need thereof effective amounts of interleukin 3 and an interferon- γ inducing polypeptide which is a polypeptide of SEQ ID NO:6 obtainable from humans, where amino acid residue 73 of SEQ ID NO:6, as represented by Xaa, is Ile or Thr, or a fragment thereof, or a homologous polypeptide thereof, wherein the fragment has substantially the same interferon- γ inducing activity as the polypeptide of SEQ ID NO:6, and the polypeptide of SEQ ID NO:6 and the homologous polypeptide thereof has the following physicochemical properties:

- (a) an amino acid sequence selected from the group consisting of SEQ ID NO:6, where amino acid residue 73 as represented by Xaa, is Ile or Thr, and a homologous sequence thereof where at least one amino acid residue in SEQ ID NO:6 is replaced with a different amino acid, or at least one amino acid residue is added to or deleted from the N-terminus and/or the C-terminus of SEQ ID NO:6, wherein said

homologous polypeptide has substantially the same physicochemical properties and biological activity as the polypeptide of SEQ ID NO:6,

(b) molecular weight

18,500 \pm 3,000 daltons on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(c) isoelectric point (pI)

4.9 \pm 1.0 on chromatofocusing;

(d) biological activity

inducing interferon- γ production by human immunocompetent cells; and

(e) acute toxicity

having an LD₅₀ of at least about one mg/kg when tested in mice.

78. A method for treating malignant tumors with antitumor immunotherapy, comprising:

culturing mononuclear cells and lymphocytes, obtained from a patient with a malignant tumor, in the presence of interleukin 2 and an interferon- γ inducing polypeptide which is a polypeptide of SEQ ID NO:6 obtainable from humans, where amino acid residue 73 of SEQ ID NO:6, as represented by Xaa, is Ile or Thr, or a fragment thereof, or a homologous polypeptide thereof, wherein the fragment has substantially the same interferon- γ inducing activity as the polypeptide of SEQ ID NO:6, and the polypeptide of SEQ ID NO:6 and the homologous polypeptide thereof has the following physicochemical properties:

(a) an amino acid sequence selected from the group consisting of SEQ ID NO:6, where amino acid residue 73, as represented by Xaa, is Ile or Thr, and a homologous sequence thereof where at least one amino acid residue in SEQ ID NO:6 is replaced with a different amino acid, or at least one amino acid residue is added to or deleted from the N-terminus and/or the C-terminus of SEQ ID NO:6, wherein said homologous polypeptide has substantially the same physicochemical properties and biological activity as the polypeptide of SEQ ID NO:6,

(b) molecular weight

18,500 \pm 3,000 daltons on sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE);

(c) isoelectric point (pI)

4.9 \pm 1.0 on chromatofocusing;

(d) biological activity

inducing interferon- γ production by human immunocompetent cells; and

(e) acute toxicity

having an LD₅₀ of at least about one mg/kg when tested in mice,

collecting cultured NK cells and LAK cells from the cultured mononuclear cells and lymphocytes; and

introducing the collected NK and LAK cells into the patient.

79. The method claim 78, wherein the malignant tumor is selected from the group consisting of colonic cancer, rectal cancer, gastric cancer, thyroid carcinoma, cancer of the tongue, bladder carcinoma, choriocarcinoma, hepatoma, prostatic cancer, carcinoma uteri, laryngeal, lung cancer, breast cancer, malignant melanoma, Kaposi's sarcoma, cerebral tumor, neuroblastoma, tumor of the ovary, testicular tumor, osteosarcoma, cancer of the pancreas, renal cancer, hypernephroma, and hemangioendothelioma, leukemia, and malignant lymphoma.

80. An isolated DNA molecule comprising a nucleotide sequence which encodes a polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:6, where amino acid residue 73, as represented by Xaa, is Ile or Thr;

(b) a contiguous fragment of SEQ ID NO:6, which fragment induces interferon- γ production in immunocompetent human cells; and

(c) a variant of (a) or (b) differing therefrom by replacement of one amino acid residue, which variant induces interferon- γ production in immunocompetent human cells.

81. The isolated DNA molecule of claim 80, wherein said nucleotide sequence encodes a polypeptide which comprises the amino acid sequence of SEQ ID NO:6, where amino acid residue 73, as represented by Xaa, is Ile or Thr.

82. The isolated DNA molecule of claim 80, wherein said nucleotide sequence encodes a polypeptide which comprises the

amino acid sequence of a contiguous fragment of SEQ ID NO:6, which fragment induces interferon- γ production in immunocompetent human cells.

83. The isolated DNA molecule of claim 80, wherein said nucleotide sequence encodes a polypeptide which comprises a variant of (a) or (b) differing therefrom by the replacement of one amino acid residue, which variant induces interferon- γ production in immunocompetent human cells.

84. A replicable recombinant DNA molecule comprising the nucleotide sequences of a self-replicable vector and a DNA molecule according to claim 80.

85. The replicable DNA molecule according to claim 84, which comprises the nucleotide sequence of SEQ ID NO:5.

86. The replicable recombinant DNA molecule according to claim 84, wherein said vector is a plasmid vector.

87. A host cell transformed with the replicable recombinant DNA molecule according to claim 84.

88. The transformed host cell according to claim 87, wherein the replicable recombinant DNA molecule comprises the nucleotide sequence of SEQ ID NO:5.

89. The transformed host cell according to claim 87, wherein said host cell is a microorganism of the species *Escherichia coli*.

90. A process for preparing a human interferon- γ inducing polypeptide, comprising the steps of:

(a) culturing in a nutrient culture medium the transformed host cell according to claim 87 to produce a human interferon- γ inducing polypeptide; and

(b) collecting the produced human interferon- γ inducing polypeptide from the resultant culture.

91. The process according to claim 90, wherein the human interferon- γ inducing polypeptide produced is purified by one or more techniques selected from the group consisting of concentrating, salting out, dialysis, separatory sedimentation, gel filtration chromatography, affinity chromatography, chromatofocusing, gel electrophoresis, and isoelectric point electrophoresis.

92. A method for neutralizing the polypeptide of claim 1, comprising a step of contacting the polypeptide with a monoclonal antibody which binds to the polypeptide.

93. The method of claim 92 wherein said monoclonal antibody has been obtained by using an antigenic fragment of the polypeptide of claim 1.

94. A collection of hybridoma cells, which is capable of producing a mixture of different monoclonal antibodies, wherein each of said different monoclonal antibodies recognizes and binds to the polypeptide of claim 1.